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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,331	01/03/2002	Gary Christie	P30994-1C2	7738

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,331	CHRISTIE ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/3/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-5 are pending.

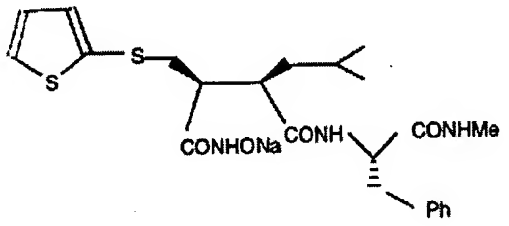
2. This application is a continuation of 09/852,807 filed 5/10/2001, which is a continuation of 09/266,050 filed 3/10/1999, which is a CIP of two applications. They are 09/101, 821 filed 9/16/1998 and 08/776, 133 filed 8/11/1997. The application 09/101,821 is a 371 of PCT/EP97/00197, which claims foreign priority to a provisional application UK 9601042.6 filed 1/17/1996. The application 08/776,133 is a 371 of PCT/EP95/02693, which claims foreign priority to a provisional application UK 9414157.9 filed 7/17/1994.

Election/Restrictions

3. Applicant has elected the following species for the elected invention (Claims 1-5):

   a. A species of inhibitor of the formulation of s-CD23 is

   [4-(N-hydroxyamino)-2-(R)-isobutyl-3-(S)-(2-thiophenethiomethyl)succinyl]-(S)-phenylalanine-N-methylamide;



4. Applicant's election with traverse of species in Paper filed 3/15/04 is acknowledged. The traversal is on the ground that the species improper because the present application is a 371 application. Thus the restriction requirement is not in accordance with the unity of invention set forth by the PCT.

This is not found persuasive because this application is not filed under 35 USC 371. It is filed under 35 USC 111(a). Thus the restriction practice under 35 USC 121 is applicable (see MPEP 1895.01 I(d)).

The requirement is still deemed proper and is therefore made **FINAL**.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted by applicant filed on 1/3/02 is acknowledged and considered as noted on PTO-1449.

Specification

6. Applicant's amendment regarding the priority claims in the first line of the specification filed 1/3/02 is acknowledged and entered.

7. The incorporation of essential material in the specification by reference to foreign applications or patents, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material

incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

8. The attempt to incorporate subject matter into this application by reference to foreign patents (e.g. WO 93/20047 on page 1, line 11, and Table on pages 7-9) is improper because the WO 92/16517 and WO 93/18173 disclose compounds that are essentials to the claimed inhibitor used in the instant method. The instant claim 1 briefly recites a method for treatment or prophylaxis of disorders comprising administering an inhibitor with the proviso that the inhibitor does not form part of the state of the art by virtue of WO 92/16517 or WO 93/18173. Thus the compounds disclose by WO 92/16517 and WO 93/18173 are essential to practice the presently claimed method.

9. The attempt to incorporate subject matter into this application by reference to foreign patents or applications (e.g. WO 93/20047 on page 1, line 11, and Table on pages 7-9) is improper because the "Table" disclose compounds that are essentials to the claimed inhibitor used in the instant method. The specification disclosure in the "Compounds disclosed" column of the "Table" recites that the compounds of these foreign patents or applications are defined in claim 1. Thus the compounds disclose by these foreign patents or applications are essential to practice the presently claimed method.

10. Claims 1-5 are treated on the merit in this Office Action.

11. Regarding the election of species, the following is noted. MPEP § 803.02 (cited in part):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

Applicant's claims were first searched to the extent of the elected species. No art was found, thus the search was extended. The art search was extended to all species and no prior art was found that anticipates or renders obvious the instant claim 4. However, the rejections below apply to the claims.

Claim Objections

12. Claims 1 and 5 are objected to because of the following informalities:

a) Claim 1 incorporates subject matter by reference to foreign patents (i.e. WO 92/16517 and WO 93/18173) is improper because the WO 92/16517 and WO 93/18173 disclose compounds that are essentials to practice the presently claimed method. Appropriate correction is required wherein the compounds disclosed by WO 92/16517 and WO 93/18173 must be included in the claim.

b) Claim 5 incorporates subject matter by reference to a Table is improper because it is unclear as to which "Table" is the claim referring to. Additionally, the inhibitors of the "Table" are essentials to practice the presently claimed method. Appropriate correction is required wherein the inhibitors disclosed by the "Table" must be included in the claim.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a written description rejection)

The presently claimed method recites a method for the treatment or prophylaxis of disorders in which the overproduction of s-CD23 is implicated. The method comprises the administration of an effective amount of an inhibitor of the formulation of human soluble CD23 to a human or non-human mammal in need with the provisos that: a) the disorder is not mediated by the matrix metalloprotease or by tissue necrosis factor; and b) the inhibitor does not form part of the state of the art by virtue of the WO92/16517 or WO93/18173.

The specification disclosure does not sufficiently teach the method of treating or preventing (prophylaxis) of disorders in which the overproduction of s-CD23 is implicated by administering an effective amount of an inhibitor. The specification description is directed to the methods of making the compounds claimed in claim 4 (pg. 10-13) and the screening methods (i.e. cell based assay and *in vitro* assay) of these compounds for its ability to inhibit the release of soluble CD23. Thus the specification is silent on the method of treating or preventing (prophylaxis) of disorders in which the overproduction of s-CD23 is implicated by administering an effective amount of an inhibitor.

The specification disclosure does not sufficiently teach the method of treating or preventing (prophylaxis) of ***any*** disorders in which the overproduction of s-CD23 is implicated with the proviso that the disorder is not mediated by the matrix metalloprotease or by tissue necrosis factor. The specification description provided a list of possible disorders that has been implicated by the overproduction of s-CD23 such as allergic diseases or rheumatoid arthritis (pg. 2, lines 11-19). Additionally, it is noted that rheumatoid arthritis is a disorder that is mediated by a matrix metalloprotease. Since rheumatoid arthritis is a disorder that is mediated by a matrix metalloprotease and is implicated by the overproduction of s-CD23, then the presently claimed method require prior knowledge of the "mechanism" of disorder (i.e. the presently claimed method require determining whether the disorder is implicated by the overproduction of s-CD23 and whether it is mediated by a matrix metalloprotease). The specification is silent on the method of determining the "mechanism' of the disorder. Thus the specification does not teach the method of treating or preventing (prophylaxis) of ***any*** disorders in which the overproduction of s-CD23 is implicated with the proviso that the disorder is not mediated by the matrix metalloprotease or by tissue necrosis factor.

The specification disclosure does not sufficiently teach the method of treating or preventing (prophylaxis) of disorders by administering an effective amount of ***any*** inhibitor of the formulation of human soluble CD23 with the proviso that the inhibitor does not form part of the state of the art by virtue of the WO92/16517 or WO93/18173. The specification description is directed to the methods of making the compounds claimed in claim 4 (pg. 10-13) and the screening methods (i.e. cell based assay and *in vitro* assay) of these compounds for its ability to inhibit the release of soluble CD23. The specification clearly does not provide an adequate

representation regarding ***any*** inhibitors that is formulated of human soluble CD23 (i.e. core structure of the inhibitor). Since no "core structure" is provided for the claimed inhibitor that use in the presently claimed method, it is unclear as what 'part of the structure' is being excluded with respect to the proviso that the inhibitor does not form part of the state of the art by virtue of the WO92/16517 or WO93/18173. Thus the specification does not teach the method of treating or preventing (prophylaxis) of disorders by administering an effective amount of ***any*** inhibitor of the formulation of human soluble CD23 with the proviso that the inhibitor does not form part of the state of the art by virtue of the WO92/16517 or WO93/18173.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the methods of making the compound claimed in claim 4 and the methods of screening these compounds for its ability to inhibit the release of soluble CD23 disclosed by the specification, the skilled artisan cannot envision the method for treatment or prophylaxis of disorders in which the overproduction of s-CD23 is implicated by administering an effective amount of an inhibitor of the formulation of human soluble CD23. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for screening it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30

USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach the method for the treatment or prophylaxis of disorders in which the overproduction of s-CD23 is implicated by administering an effective amount of an inhibitor of the formulation of human soluble CD23. Therefore, only the methods of making the compound claimed in claim 4 and the methods of screening these compounds for its ability to inhibit the release of soluble CD23, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

15. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification, while being enabled for the methods of making the compound claimed in claim 4 and the methods of screening these compounds for its ability to inhibit the release of soluble CD23; the specification does not reasonably provide enablement for the method for the treatment or prophylaxis of disorders in which the overproduction of s-CD23

is implicated by administering an effective amount of an inhibitor of the formulation of human soluble CD23. The specification does not enable any person skilled in the art to which it pertains; or with which it is most nearly connected, to use the invention as claimed commensurate in scope with these claims.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue" (See *In re Wands* USPQ 2d 1400 (CAFC 1988)). These factors include, but are not limited to:

1. The breadth of the claims.
2. The nature of the invention
3. The state of the prior art;
4. The level of one of ordinary skill
5. The level of predictability in the art;
6. The amount of direction provided by the inventor;
7. The presence or absence of working examples;
8. The quantity of experimentation necessary needed to make or use the invention based on the disclosure.

(1-2) The breadth of the claims and the nature of the invention:

The claims are directed to the method for the treatment or prophylaxis of disorders (diseases) in which the overproduction of s-CD23 is implicated by administering an effective amount of an inhibitor of the formulation of human soluble CD23.

The claims are broad enough to encompass both "protecting" of ***any*** destruction prior to ***any*** disease onset (e.g. PREVENTION) and during/subsequent to ***any*** disease onset (e.g. TREATMENT) wherein the overproduction of s-CD23 is implicated.

(3 and 5) The state of the prior art and the level of predictability in the art:

Claims drawn to pharmaceuticals and methods of treatment generally require supporting data because of the unpredictability in biological responses to therapeutic treatments. This is especially true for a preventive method, which meets with stricter scrutiny than treatments, since additional controls and testing must be performed to insure prevention. The burden of enabling the prevention of a disease or its symptoms (i.e. the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those mammals (e.g. humans) susceptible to such diseases and the difficulty of proof that the administration of the drug composition was the agent that acted to prevent the condition. The specification does not provide guidance as to how one skilled in the art would go about screening those mammals susceptible to a disorder wherein the overproduction of s-CD23 is implicated. Nor is guidance provided in the specification as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed composition in preventing the disease wherein the overproduction of s-CD23 is implicated. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

For, the efficacy of a drug treatment in vivo faces unfavorable obstacles not present in vitro models. As such, in vivo utility necessarily involves unpredictability with respect to physiological activity of an asserted process in humans. See discussion in Ex parte Kranz, 19 USPQ2d 1216,1218-1219 (6/90). For example, drug delivery to the targeted area must survive

the acidic environment of the stomach if administered orally. Additionally, the delivery of the drug across necessary cell surfaces in amounts needed to be efficacious, but not lethal to the organism, necessitates sensitive testing in order to adequately determine the proper human dosage.

Additionally, there are no mammalian (e.g. human) genetic markers to enable screening of those mammals genetically predisposed toward ***any*** disease wherein the overproduction of s-CD23 is implicated.

Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

(4) The level of one of ordinary skill in the art:

The level of skill would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples.

The specification only provides support (e.g. examples) for the methods of making the compound claimed in claim 4 and the methods of screening these compounds for its ability to inhibit the release of soluble CD23 in biochemical assays. There are no examples presented which would be deemed by one of ordinary skill in the art to be correlatable toward PREVENTION of the onset of the disease or the TREATMENT of the disease wherein the overproduction of s-CD23 is implicated.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

Thus, the specification discloses only limited examples and in light of the unpredictability and inability of others to effect prevention of disease or its symptoms, further

examples which are reasonably predictive of *in vivo* preventative utility are needed in order to provide the requisite enablement for the presently claimed invention as claimed.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 8 of U.S. Patent No. 6,235,753 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the recited claims in the patent and present application encompass the same method steps with the exception of the steps of the provisos that: a) the disorder is not mediated by the matrix metalloprotease or by tissue necrosis factor; and b) the inhibitor does not form part of the state of the art by virtue of the WO92/16517 or WO93/18173. Thus the methods would be obvious over each other.

18. Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent No. 6,458,779 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the recited claims in the patent and present application encompass the same method steps with the exception of the steps of the provisos that: a) the disorder is not mediated by the matrix metalloprotease or by tissue necrosis factor; and b) the inhibitor does not form part of the state of the art by virtue of the WO92/16517 or WO93/18173. Thus the methods would be obvious over each other.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
June 10, 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER